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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,879	04/09/2007	**Augustinus Bader**	50326/006001	8676

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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

NOTIFICATION DATE	DELIVERY MODE
06/28/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/583,879	BADER, AUGUSTINUS	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36 and 39-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36 and 39-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/3/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03 May 2010 has been entered.

Status of Application, Amendments and/or Claims

The amendment and Applicant's arguments, filed 03 May 2010, have been entered in full. Claims 1-35, 37 and 38 are canceled. Claims 36, 39 and 40 are amended. New claims 41-44 are added. Claims 36, 39-44 are under examination.

Information Disclosure Statement

The information disclosure statement(s) (IDS) (filed 03 May 2010) was received and complies with the provisions of 37 CFR §§1.97, 1.98 and MPEP § 609. It has been placed in the application file and the information referred to therein has been considered as to the merits.

Withdrawn Objections And/Or Rejections

The rejection to claims 1, 3, 5, 12, 13, 36, 38 and 39 under 35 U.S.C. 102(e) as being anticipated by Brines et al., US 2003/0104988 A1, as set forth at pages 2-4 of the previous Office Action (03 November 2009), is *withdrawn* in view of the discussion

during the phone Interview between Applicants and the Examiners (07 April 2010) and the amendment (03 May 2010).

The rejection to claims 6 and 40 under 35 U.S.C. 103(a) as being unpatentable over by Brines et al., US 2003/0104988 A1 as applied to claims 1 and 36 and further in view of Bhaskaran et al. United States Patent Application Publication US 2004/0136952 A1, as set forth at pages 4-6 of the previous Office Action (03 November 2009), is *withdrawn* in view of the discussion during the phone Interview between Applicants and the Examiners (07 April 2010) and the amendment (03 May 2010).

The rejection to claims 36-40 under 35 U.S.C. 112, first paragraph, written description (new matter), as set forth at pages 6-8 of the previous Office Action (03 November 2009), is *withdrawn* in view of the amendment (03 May 2010).

The rejection to claim 36 under 35 U.S.C. 112, second paragraph, as set forth at page 8 of the previous Office Action (03 November 2009), is *withdrawn* in view of the amendment (03 May 2010).

NEW CLAIM REJECTIONS/OBJECTIONS

Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 36, 39 and 40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method for healing of burn wounds in an individual using a skin graft, the method comprising **topically applying erythropoietin (EPO) to said wound**,

does not reasonably provide enablement for:

a method for healing of burn wounds in an individual using a skin graft, the method comprising **topically applying erythropoietin (EPO) to said skin graft, then applying said skin graft to said wound**.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The instant specification teaches that in 8 burned patients, the donor site of the skin graft healed 50% more quickly upon administration of EPO (para 0185). It is well known to those skilled in the art that bacterial infection can be life-threatening in burn victims. Maggi et al. (Burns Vol. 25:237-241, 1999) teach that new epithelium is very vulnerable to desiccation or lysis (pages 237-238). Maggie et al. teach the use of a non-cytotoxic antibacterial solution which is topically applied ***after*** the skin is grafted onto the subject. The instant specification is not enabling for the full scope of the claims because it fails to teach examples of EPO being topically administered to a skin graft *in vitro*, which is then grafted to a wound on a patient. The specification fails to teach parameters such as the osmality of topically applied EPO. For example, Maggie et al. teach that mafenide acetate cream has been available for 20 years and has been effective in decreasing burn wound sepsis but the osmolality of the cream causes desiccation and is cytotoxic to fresh keratinocytes, therefore it is not useful as a topical

agent for fresh autografts (page 240, Discussion). Surely, an *in vitro* skin graft would be more delicate and susceptible to desiccation versus skin which has been grafted on the patient. The specification fails to teach the amount of time (i.e. time window) the topically applied EPO stays on the skin graft before it is grafted on the burn patient. For example, is there a minimum amount of time the topically applied EPO must stay on the *in vitro* skin graft before it can be grafted on the burn patient? Is there a maximum amount of time before the *in vitro* skin graft and topically applied EPO are no longer effective?

Due to the large quantity of experimentation necessary to topically administer EPO to a skin graft *in vitro* and apply said skin graft on a burn wound without using specific parameters, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite limitations regarding time windows of administration and suitable parameters to achieve the recited goal, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 36, 39 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buemi et al. (Acta Derm Venereol. 82:411-417, 2002) in view of Kim et al. (Journal of Burn Care & Rehabilitation, 14(5):541-3; Sept-Oct 1993), Brines et al. (Reference of record) US 2003/0104988 A1) and Bhaskaran et al. (Reference of record; United States Patent Application Publication US 2004/0136952 A1).

Buemi et al. teach the topical administration of EPO in cutaneous flap animal models (cutaneous skin fragments are cut from the animal model, Material and Methods; pages 411-412). Buemi et al. teach that rHuEPO treated rats had an increased number of capillaries and neoangiogenesis. Buemi et al. teach that their observations suggest a role for EPO in vasoproliferative and neoangiogenic processes and in wound healing. Buemi et al. teach that rHuEPO administration can improve the wound-healing process in both early and late stages of injury (Discussion; pages 415-416). Buemi et al. do not teach topically administering EPO to burn wounds, additional glycosylation sites in EPO or EPO which is conjugated to polyethylene glycol (PEG).

Kim et al. teach the admission of a woman with 18% of her body covered with burns. The patient under went excision and skin grafting on the burned area. Kim et al. teach the subcutaneous injections of EPO (page 541, last paragraph-page 542). Kim et al. teach that operations are carefully staged to minimize blood loss that accompanies excision and grafting.

Brines et al. teach the use of EPO for protecting, maintaining, enhancing or restoring the function or viability of EPO-responsive mammalian cells and their associated cells, tissues and organs. Brines et al. teach EPO administration (abstract;

paragraphs 0005 and 0024). Brines et al. teach the use of EPO glycosylation variants such as EPO with additional glycosylation sites (paragraphs 0008, 0009 and 0064).

Bhaskaran et al. teach the conjugation between PEG and various proteins such as EPO (abstract; paragraphs 0003, 0021 and claims). Bhaskaran et al. teach that the attachment of PEG to proteins have been shown to stabilize the protein, improve the bioavailability and/or reduce the immunogenicity *in vivo* (paragraphs 0007, 0017-0019). Bhaskaran et al. teach that the coupling of the polymer near one or more glycosylation sites mimics the beneficial effects of glycosylation of the protein (paragraphs 0023, 0095, 0099).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify a method of healing dermal wounds *in vivo* by topically administering EPO to said wounds as taught by Buemi et al. by applying it topically to treat burns wounds wherein EPO has additional glycosylation sites and is conjugated with PEG as taught by Brines et al. and Bhaskaran et al. (respectively) with a reasonable expectation of success. The motivation and expected success is provided by Buemi, Kim, Brines and Bhaskaran. Buemi et al. teach that rHuEPO administration can improve the wound-healing process in both early and late stages of injury. Kim et al. teach that EPO is used to prevent blood loss in burn patients. It would be obvious to also apply EPO to burn wounds because EPO has been shown to improve the wound-healing process and induce vasoproliferative/neoangiogenic processes. Additional glycosylation sites and pegylation, as taught by Brines et al. and Bhaskran et al., are

known to increase the half-life and stability of a protein *in vivo*. It would be obvious to one of skill in the art to utilize a stable EPO pharmaceutical with a long half-life.

Claims 41-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buemi et al. (Acta Derm Venereol. 82:411-417, 2002) in view of Dunn, J.M. (Abstract; Clinics in podiatric medicine and surgery, Vol. 4/No. 2, pages 413-418, April, 1987), Brines et al. (Reference of record) US 2003/0104988 A1) and Bhaskaran et al. (Reference of record; United States Patent Application Publication US 2004/0136952 A1).

Buemi et al. teach the administration of EPO in cutaneous flap animal models (cutaneous skin fragments are cut from the body in the animal model, Material and Methods; pages 411-412). Buemi et al. teach that rHuEPO treated rats had an increased number of capillaries and neoangiogenesis. Buemi et al. teach that their observations suggest a role for EPO in vasoproliferative and neoangiogenic processes and in wound healing. Buemi et al. teach that rHuEPO administration can improve the wound-healing process in both early and late stages of injury (Discussion; pages 415-416). Buemi et al. do not teach mechanical debriding of wounds, additional glycosylation sites in EPO or EPO which is conjugated to PEG.

Dunn teaches the use of mechanical debridement in dermal wounds to remove necrotic and devitalized tissue. Dunn teaches that the process helps with effective wound healing and decreases the risk of infection.

Brines et al. teach the use of EPO for protecting, maintaining, enhancing or restoring the function or viability of EPO-responsive mammalian cells and their associated cells, tissues and organs. Brines et al. teach EPO administration (abstract; paragraphs 0005 and 0024). Brines et al. teach the use of EPO glycosylation variants such as EPO with additional glycosylation sites (paragraphs 0008, 0009 and 0064).

Bhaskaran et al. teach the conjugation between PEG and various proteins such as EPO (abstract; paragraphs 0003, 0021 and claims). Bhaskaran et al. teach that the attachment of PEG to proteins have been shown to stabilize the protein, improve the bioavailability and/or reduce the immunogenicity *in vivo* (paragraphs 0007, 0017-0019). Bhaskaran et al. teach that the coupling of the polymer near one or more glycosylation sites mimics the beneficial effects of glycosylation of the protein (paragraphs 0023, 0095, 0099).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify a method of healing dermal wounds *in vivo* by topically administering EPO to said wounds as taught by Buemi et al. and the method of mechanical debridement as taught by Dunn, by employing an EPO with additional glycosylation sites and conjugated with PEG as taught by Brines et al. and Bhaskaran et al. (respectively) with a reasonable expectation of success. The motivation and expected success is provided by Buemi, Dunn, Brines and Bhaskaran. Buemi et al. teach that rHuEPO administration can improve the wound-healing process in both early and late stages of injury and induce vasoproliferative/neoangiogenic processes. It would be obvious to use mechanical debridement, as taught by Dunn, to remove dead tissue

and old blood from a wound. Additional glycosylation sites and pegylation, as taught by Brines et al. and Bhaskran et al., are known to increase the half-life and stability of a protein *in vivo*. It would be obvious to one of skill in the art to utilize a stable EPO pharmaceutical with a long half-life.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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6/17/10